

C1  
cont.

- (iii) cleaving each fragment in a mass spectrometer to release its mass label; and
  - (iv) determining each mass label by mass spectrometry to relate the feature of each fragment to the length of the fragment in order to characterize said DNA
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C2

21. (Twice Amended) A method for characterising DNA, which comprises
- (a) providing a primed DNA single-stranded template;
  - (b) contacting the template in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the templates in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but reversibly blocked to prevent further polymerisation thereto, wherein the step of contacting forms a series of templates containing all possible lengths of the second strand of DNA, each second strand terminated with one of the probes;
  - (c) removing unincorporated nucleotides;
  - (d) unblocking the modified nucleotides;
  - (e) contacting the series of templates with an array of oligonucleotide probes to form a series of fragments, each oligonucleotide probe having a nucleotide sequence of common length 2 to 6, and all combinations of sequences being present in the array, wherein each probe is cleavably attached to a mass label uniquely resolvable in mass spectrometry for identifying the nucleotide sequence;

(f) separating the fragments by capillary electrophoresis, thereby determining the length of each fragment;

(g) cleaving each fragment to release its mass label; and

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Cont.  
(h) determining each mass label by mass spectrometry to relate a nucleotide sequence that corresponds to the mass label to a position in the template so as to deduce the sequence of the template in order to characterise the DNA.

22. (Twice Amended) A method for characterising DNA, which comprises

(a) providing a plurality of primed DNA single-stranded templates, each at a unique concentration;

(b) contacting the templates in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the templates, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the templates in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but reversibly blocked to prevent further polymerisation thereto, wherein the step of contacting forms a series of templates containing all possible lengths of the second strand of DNA, each second strand terminated with one of the probes;

(c) removing unincorporated nucleotides;

(d) unblocking the modified nucleotides;

(e) contacting the series of templates with an array of oligonucleotide probes to form a series of fragments, each oligonucleotide probe having a nucleotide sequence of

common length 2 to 6, and all combinations of sequences being present in the array, wherein each probe is cleavably attached to a mass label uniquely resolvable in mass spectrometry for identifying the nucleotide sequence;

(f) separating the fragments by capillary electrophoresis, thereby determining the length of each fragment;

(g) cleaving each fragment to release its mass label; and

(h) determining the identity and amount of each mass label by mass spectrometry to relate a nucleotide sequence of a probe that corresponds to the mass label to a position in its respective template so as to deduce the sequence of the template in order to characterise the DNA.

23. (Twice Amended) A method for characterising DNA, which comprises

(a) providing a primed DNA single-stranded template;

(b) contacting the template in the presence of DNA ligase with a mixture of oligonucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, the oligonucleotides each having a common length in the range 2 to 6, wherein the mixture further comprises a set of probes containing all possible oligonucleotides of the common length L for hybridising to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a corresponding mass label uniquely resolvable in mass spectrometry for identifying the modified oligonucleotide, wherein the step of contacting

forms a series of fragments containing all possible lengths of the second strand of DNA of integer multiples of L, each fragment terminated with one of the probes;

(c) separating the fragments [from one another on the basis of their length] by capillary electrophoresis, thereby determining the length of each fragment;

(d) cleaving each fragment to release its mass label; and

(e) determining each mass label by mass spectrometry to relate its corresponding oligonucleotide to a position in the template so as to deduce the sequence of the template in order to characterise the DNA.

24. (Twice Amended) A method for characterising DNA, which comprises

(a) providing a plurality of primed DNA single-stranded templates, each at a unique concentration;

(b) contacting the templates in the presence of DNA ligase with a mixture of oligonucleotides for hybridising to the templates for forming a second strand of DNA complementary to the templates, the oligonucleotides each having a common length in the range 2 to 6, wherein the mixture further comprises a set of probes containing all possible oligonucleotides of the common length L for hybridising to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a corresponding mass label uniquely resolvable in mass spectrometry for identifying the modified oligonucleotide, wherein the step of contacting

forms a series of fragments containing all possible lengths of the second strand of DNA of integer multiples of L, each fragment terminated with one of the probes;

(c) separating the fragments by capillary electrophoresis, thereby determining the length of each fragment;

(d) cleaving each fragment to release its mass label; and

(e) determining the identity and amount of each mass label by mass spectrometry to relate its corresponding oligonucleotide to a position in its respective template so as to deduce the sequence of the template in order to characterise the DNA.

C2  
C3

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27. (Once Amended) A method for characterizing DNA, which comprises:

(a) providing at least one DNA single-stranded template primed with a primer;

(b) generating a population of fragments of said DNA from the at least one template by contacting the at least one template in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the at least one template for forming a second strand of DNA complementary to the at least one template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the at least one template in which the nucleotide of each probe comprises a modified nucleotide or oligonucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto, which modified nucleotide or oligonucleotide is cleavably attached to the mass label for identifying the modified nucleotide or oligonucleotide, which mass label is cleavable from the probe in a mass spectrometer and is resolvable by mass spectrometry, and wherein each fragment is terminated with one of the probes, wherein the

population comprises at least one series of DNA fragments, the or each series containing all possible lengths of a second strand of DNA complementary to the or each template;

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cont.  
(c) separating the fragments by capillary electrophoresis, thereby determining the length of each fragment;

(d) cleaving each fragment in a mass spectrometer to release its mass label; and

(e) determining each mass label by mass spectrometry to relate a terminating modified nucleotide or oligonucleotide of each fragment to the length of the fragment in order to characterize said DNA.

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